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## Ponderosa Pine Needle-Induced Parturition in Cattle<sup>1</sup>

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Needles of the Ponderosa pine ABSTRACT: (Pinus ponderosa) induce premature parturition in cattle when ingested during late pregnancy, especially during the third trimester. The closer to term, the more likely that pine needles will induce parturition. Experiments were designed describe the clinical signs and behavior associated with ingestion of pine needles. Pine needles adversely affected only pregnant cows and did not seem to affect nonpregnant, cycling cows, sheep, goats, or rabbits. Premature parturition was more likely if cows ingested the needles after the 8th mo of pregnancy, if they ingested pine needles over a

period of 3 d or more, and if cows ate a relatively large amount of pine needles (about 2.2 to 2.7 kg/d). A synthetic progesterone, melangesterol acetate, and a prostaglandin inhibitor (ketoprofen) seemed to be of some prophylactic benefit; however, further research is required to assess the practicality of the approach and the magnitude of the benefit. Ponderosa pine bark and new-growth branch tips, which seem to be more potent inducers of premature parturition, may be useful in the extraction and identification of the parturifacient component(s).

Key Words: Cattle, Abortion, Poisonous Plants, Pine Needles, Toxicity

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#### Introduction

Needles from the Ponderosa pine have been known to induce premature parturition or abortion in cattle since the early part of this century (Bruce, 1927). McDonald (1952) experimentally induced premature parturition in cows by feeding needles from the Ponderosa pine. Early folklore reports the use of teas of Ponderosa pine as an abortifacient in women (Tucker, 1961). Numerous feeding experiments have been conducted and field cases have been reported that further describe and characterize the clinical effects observed in pregnant cows fed pine needles (Stevenson et al., 1972; James et al., 1977, 1989). From 1960 to 1980, research concerned feeding

James et al. (1989) reviewed research at the USDA/ARS Poisonous Plant Research Laboratory from 1973 to 1984. Results of feeding trials indicate cows' susceptibility to the abortifacient action of PN and that the content and concentration of the toxicants in the pine trees vary.

Since 1984, cooperative research has attempted to elucidate the parturifacient compounds in the needles, to determine the site of action and mechanism in the cow, and to clarify the environmental conditions and cattle behavior that prompt consumption of PN.

This report reviews the current literature concerning description and toxicology of the plant and clinical signs of the induced parturition,

extracts and fractions from pine needles (PN) to small animals. Since 1980 additional research has involved cattle, the only animal species in which PN induces parturition. This has generally been referred to as PN abortion; however, research and field reports have shown it is usually a premature parturition in which the live calf soon dies due to complications associated with premature birth (James et al., 1989). Calves born late in the last trimester,  $\geq$  250 d of gestation, may survive given the proper care.

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mechanisms of toxicity, conditions favoring toxicity, and characteristics of the toxic agent.

# Description and Distribution of Ponderosa Pine

Ponderosa pine is one of the most prevalent and is the most widely distributed *Pinus* species in the western United States (Van Hooser and Keegan, 1988). Ponderosa pine forests extend from southern British Columbia in Canada into Mexico, and from the Pacific coast along the California-Oregon border to western Nebraska. Ponderosa pine is the principal lumber species on some 11 million hectares in the western United States (USDA, 1982), and in terms of acres where ponderosa predominates it is second only to the Douglas fir.

In the western United States, the heaviest concentrations of Ponderosa pine occur in northern California (2 million hectares), eastern Oregon (2 million hectares), Arizona (1.3 million hectares), New Mexico (1.3 million hectares), and the Black Hills of South Dakota (.5 million hectares). The remaining western states contain substantial areas of Ponderosa pine, although the species is not the dominant type (Van Hooser and Keegan, 1988).

Ponderosa pine is adaptable to various climates, elevations, and soil types. Even though ideal conditions include wet, deep, sandy gravel and clay loams with pH between 6.0 and 7.0, the pine grows in a variety of soil types and where pH ranges from 4.9 to 9.1 and at elevations ranging from sea level around Tacoma, WA to 3,048 m in the southern Sierra Nevadas. Ponderosa pine requires adequate moisture and temperatures that are not too extreme (Van Hooser and Keegan, 1988).

Ponderosa is a three-needled pine, although groups of two needles can also be found on a tree. The average tree in the northern extreme of its range has a diameter of 40.6 cm and a height of 18.3 m. In Arizona and New Mexico trees average 27.9 cm in diameter by 12.5 in height. Average Ponderosa pine in the Black Hills of South Dakota have a diameter of 27.9 cm and a height of 14.3 m. Trees 1.2 to 1.8 m in diameter and 61 m tall are not uncommon in Montana, northern Idaho, and California (Van Hooser and Keegan, 1988).

Common names reflect bark color. Young, vigorous trees tend to have dark brown to nearly black bark, and are commonly known as "black jack" pine. Older, less vigorous specimens have lighter, yellowish bark and are called "yellow pine."

Throughout the western United States, Ponderosa pine is the fourth most plentiful lumber species behind Douglas fir, western hemlock, and

other firs. Ponderosa pine accounts for approximately 35,000 jobs and one billion dollars in economic activity annually in terms of harvesting, hauling, processing, marketing, and management (Van Hooser and Keegan, 1988). The aesthetic and economic importance of this pine means it is probably not feasible to eliminate the Ponderosa pine from some of our important rangelands. We must learn to manage cattle and learn how to prevent PN-induced abortion in these areas so that people raising cattle can utilize the valuable forage among the trees.

# Toxicology and Description of the Induced Parturition

The primary toxicological response in pregnant cattle ingesting PN is early parturition and subsequent complications such as retained fetal membranes, pyometria, septic metritis, toxemia, and death (Stevenson et al., 1972). Occasionally, toxicity may be manifested by depression, respiratory distress, and decreased appetite, followed by premature parturition, postpartum complications, and death.

The preparturient signs are characterized by weak uterine contractions, sometimes incomplete cervical dilation, excessive uterine hemorrhage, and mucus. After PN-induced parturition, the placenta is almost always retained, and the uterus is often atonic and filled with fluid, placental debris, and blood. Septic metritis is frequent and may be followed by peritonitis and death if the cow does not receive prompt veterinary therapy (James et al., 1989). Early antibiotic treatment after parturition will generally avoid life-threatening complications and the fetal membranes will be spontaneously lost within 10 to 15 d.

When cows ingest PN during the last trimester of pregnancy, calves are usually born alive. The closer to term, the more likely a calf will survive. Calves born after 250 d gestation may survive with extra care.

### **Pathology**

Pathological changes in tissues from calves necropsied after PN-induced parturition were not considered to be primarily due to maternal ingestion of PN. Likewise, changes in maternal tissue in cows that died after induced parturition were not considered specific to PN consumption (Stuart et al., 1989). Postmortem autolysis was considered more rapid than normal in these cows but was believed to be associated with pyrexia and the septicemia.

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Extensive vasoconstriction of the caruncular vascular bed with accompanying necrosis and hemorrhage have been reported, but there was no histological evidence of bacterial infection or fungal growth (Stuart et al., 1989). Ford et al. (1992) suggested that this vasoconstriction may be the mode of action of the PN toxicant in the induced parturition.

Jensen et al. (1989) reported histopathological changes in the placenta and corpora lutea (CL) of pregnant cows that ate PN. Reduced numbers of binucleate, trophoblastic giant cells in the placentomes and increased numbers of necrotic luteal cells in CL in these cows was believed to be associated with PN consumption. These changes occur in normal or induced parturition and these results were not compared with controls at the same stage of pregnancy or parturition. Therefore, the exact site of action of the PN is not known, nor is it known whether any histological lesion can aid in the diagnosis of PN toxicity.

### **Physiological Considerations**

Research conducted during the last 6 to 8 vr has broadened our knowledge of the mechanisms underlying PN-induced premature parturition. In 1982 and 1983, daily blood samples were collected from pregnant cows fed PN at the Poisonous Plant Research Laboratory, Logan, UT. Subsequent serum hormone analyses for estradiol, progesterone, and cortisol were completed at the Livestock and Range Research Station in Miles City, MT (Short et al., 1989a). Changes in cortisol were attributed to the stress of handling and parturition. Estradiol was elevated after feeding PN, but concentrations by day of parturition were similar to those in controls. Progesterone concentrations increased in cows fed PN; maximum concentrations were observed 4 to 8 d after initiation of PN feeding. A subsequent sharp decline in progesterone was associated with induced parturition and was similar to that associated with normal parturition (Short et al., 1989a).

The elevated serum progesterone after ingestion of PN and its relationship to induced parturition is still not clearly understood. Short et al. (1989c) suggested that the increase in progesterone could be attributed to one or a combination of three factors: 1) increased progesterone production by the CL, 2) increased progesterone production by the placenta and(or) adrenal glands, and 3) decreased metabolic clearance of progesterone. When nonpregnant, cycling cows were fed PN beginning on d 8 of a synchronized estrous cycle until estrus, PN did not affect estrous behavior, estrous cycle length, or progesterone profiles

(Staigmiller and Panter, 1985). Therefore, PN apparently did not affect the CL in the nonpregnant, cycling cow, but it was not known whether it affected the CL during pregnancy. To further differentiate the role of the CL in PN-induced parturition, Phelps et al. (1987) divided 32 pregnant cows into four groups of eight cows each. Two groups were injected with  $PGF_{2\alpha}$  (Lutalyse, Upjohn, Kalamazoo, MI) on d 236 and 237 of gestation to regress the CL. One CL-regressed group and one control group (no Lutalyse) were fed 2.0  $kg \cdot cow^{-1} \cdot d^{-1}$  of PN starting on d 250 of gestation. The premature parturition induced by PN was not affected by the absence of the CL (Phelps et al., 1987). These two experiments support the hypothesis that PN probably exerts its effects at the fetal/ placental level.

Short et al. (1989b) studied the effects of MGA (melangesterol acetate, Upjohn, Kalamazoo, MI, a synthetic progesterone analog absorbed by the intestines) and Ketoprofen (2-l3-benzoylphenyllpropionic acid), a prostaglandin inhibitor. Both compounds delayed the PN-induced premature parturition. Prolonged administration of MGA increased the incidence of stillborn calves. These results suggest that PN-induced premature parturition may involve a prostaglandin mechanism acting on the source of progesterone.

The fetus is believed to initiate parturition. In normal circumstances parturition is probably determined by the size and maturity of the fetus, fetal nutrient demand, and the ability of the dam to supply enough blood for continued in utero development. The incidence of PN-induced parturition is greatest during the last trimester of pregnancy, although abortions have occurred earlier (Stevenson et al., 1972; James et al., 1977). Short et al. (1989c) reported that cows fed 2.7 kg of ground PN-cow<sup>-1</sup>·d<sup>-1</sup> beginning at gestation d 116, 167, 215, and 254 had an abortion incidence of 0, 38, 50, and 100%, respectively.

Christenson et al. (1992b) found vasoactive components in the plasma of cows fed PN. Plasma from cows fed PN was perfused in vitro through a caruncular arterial bed of an isolated bovine placentome. Caruncular arterial pressure and response to potassium stimulation increased in a dose-dependent manner as the concentration of plasma from PN-fed cows increased. This vasoactive response increased progressively during the last 3 d of PN feeding before parturition was induced. Subsequently, Christenson et al. (1992a) demonstrated a 56.9% reduction in uterine arterial blood flow to the gravid horn of pregnant cows fed PN  $(2.7 \text{ kg} \cdot \text{cow}^{-1} \cdot \text{d}^{-1})$  from d 250 to 258 of gestation; premature parturition occurred on d 259. Ford et al. (1992) speculated that PN-induced premature parturition in cows occurs by reducing

the secretion of catechol estrogens by the gravid uterus, thus increasing uterine arterial tone, and subsequently reducing uterine arterial blood flow. The rapid increase in size of the fetus and the associated increase in fetal demands on placental exchange of nutrients and waste products would require optimal blood flow for pregnancy to continue. Thus, vasoconstriction or reduced blood flow late in gestation could be a key mechanism in the induction of early parturition by PN.

### **Identification of the Toxic Agent**

Little is known about the parturifacient agent(s) derived from PN. Many fractions and crude extracts obtained by numerous methods have been tested in rodents but have not been directly applied to the bovine. Allen and Kitts (1961) found that aqueous fractions of PN had anti-estrogenic effects when mixed with the feed of mice, which was verified by Allison and Kitts (1964) and Cook and Kitts (1964). Call and James (1978), however, did not demonstrate any adverse effects of PN in sheep. Wagner and Jackson (1983) reported that PN contained a phytoestrogen, which they verified by an aqueous extract in a mouse uterine cytosol assay. Others have reported that PN extracts from different solvent systems have variable effects on reproduction in mice (Chow et al., 1972; Cogswell, 1974; Anderson and Lozano, 1977; Kubik and Jackson, 1981; Wagner and Jackson, 1983). None of these fractions has been fed to cows.

The parturifacient properties of PN may be affected by heat, as suggested by pelleting with steam, which reduced the ability of PN to induce premature parturition (Tucker, 1961; Anderson and Lozano, 1979; Short et al., 1987).

Certain factors on PN may induce reproductive failure. A bacterium, Listeria monocytogenes, which induces abortion, may be a factor in PN-induced parturition (Adams et al., 1979). Mycotoxins have been implicated as the parturifacient agent (Chow et al., 1974; Anderson and Lozano, 1977, 1979). No histological evidence supports the hypothesis that bacteria or mycotoxins induce parturition (Stuart et al., 1989). These factors affected parturition in rodents but not in cattle. Panter et al. (1991) analyzed levels of nine mycotoxins in PN collections that induced early parturition; levels of all mycotoxins were below detectable limits.

Other components of the Ponderosa pine tree are more potent than PN in the induction of parturition. Pine bark and the new-growth tips of branches consistently induced parturition within 2 to 5 d (Panter et al., 1990). If these materials contain higher concentrations of the putative

compound than pine needles, they may facilitate isolation and extraction of the parturifacient.

### **Implications**

Ponderosa pine needle-induced parturition causes substantial financial losses to the livestock producers in the western United States each year. Estimated losses range from \$4.5 million to \$20 million annually to the cattle industry. These losses can be reduced through research to better understand the condition and to develop management strategies or treatments. This type of research will also advance our understanding of the mechanism of normal parturition, treatment of premature births, and treatment of related postpartum complications. Currently, there are no clinical or histopathological data to support positive diagnoses of pine needle-induced abortion in cattle. Therefore, additional study of the histopathological, histochemical, physiological or biochemical changes after the ingestion of pine needles is warranted.

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